Iranian Journal of Radiology
Volume 18 · Issue 4 · e111481

OPEN PEER REVIEW

Use of an Easily Applicable Thyroid Imaging-Reporting and Data System (TI-RADS): Our Kwak TI-RADS Experience

Mahmut Corapli, Burcin Pehlivanoglu, Hüseyin Alakus, Haci Taner Bulut

SUBMITTED	REVISED	ACCEPTED	DOI
22 Nov 2020	7 Sep 2021	11 Sep 2021	10.5812/iranjradiol.111481

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1, Referee 2, Associate Editor, Editor-in-Chief 2
2 **Revision 1** Referee 1, Referee 2, Associate Editor, Editor-in-Chief 4
Authors' reply to reviewers 5
Reviewer and editor comments 13
3 **Revision 2** Editor-in-Chief 14
Authors' reply to reviewers 15
Reviewer and editor comments 16

1 Original submission

4 comments · 5 Dec 2020 – 26 Apr 2021

Referee 1 Reviewer

MINOR REVISION 5 Dec 2020

From a methodological point of view, this manuscript is relatively well written; however, it needs some revisions as follows:
1. Each abbreviation, such as US, must be written out in full at first use.
2. The study design is cross-sectional, and this must be stated in the first sentence of the methods section in both the abstract and the full text.
3. Inclusion and exclusion criteria must be described in detail in the methods section.
4. The demographic characteristics of the patients must be presented in the first paragraph of the results.
5. In table 1, the demographic characteristics of all patients must be presented.
6. In table 2, rather than presenting p-values for the univariate and multivariate analyses, it is better to use odds ratios (ORs) along with 95% confidence intervals; moreover, ORs must also be presented in the results text. Finally, the coefficient of determination (R2) for the multivariate model must be reported below table 2.

Referee 2 Reviewer

REJECT 21 Apr 2021

This paper does not meet the requirements for publication for the following reasons:

1-The correlation between TIRADS based on radiologic evaluation and histopathologic findings has already been examined in multiple studies with larger sample sizes than this study, indicating that the risk of malignancy increases as the TIRADS score increases.

2-What is the rationale for this study, which has a smaller sample size and especially fewer malignant nodules compared to previous studies? Since the number of malignant nodules (only 42) is extremely low, the results of this study do not meet the requirements for publication.

3-Other than the lack of novelty and smaller sample size compared to previous studies, there are some other concerns in this paper that I would like the authors to take into consideration:

Methods
Radiologic Characterization of Nodules:
-Paragraph 1, sentence 3:
The sentence " However, the contribution of size to malignancy and when the nodule was not followed up ,the contribution of difference in size to malignancy was not investigated " is not clear to
readers.
-Paragraph 1, sentence 11:
The phrase " Their shapes were grouped based as taller then wide and taller then wide based on the length of their
vertical and horizontal axes" should be rephrased to use taller than wide and wider than tall instead.

Results:
Paragraph 1, sentence 2:
What do the authors mean by "80 patients with Bethesda 3 (AUS-FLUS) and 4 lesions were excluded from statistical
analysis"?
Paragraph 3, sentences 1-4:

The authors stated, "In univariate analysis ,the presence of solid component ,hypoechogenicity, and microlobulated or irregular margins ,microcalcifications and taller then wide shape were significantly associated with
malignancy". Immediately afterward, they stated, " However , only hypoechogenicity and taller then wide shape were
found to have significant association with malignancy".
I think the authors should add multivariate analysis before the latter sentence.

Discussion:
Paragraph 1, sentences 2 & 3:
The authors stated that " The difference with Kwak TIRADS was that it included the vascularization of the nodule ". In the methods, the authors indicated that they used Kwak TIRADS in this study; however, I did not see any results
based on vascularization of the nodules in this study.

Associate Editor

MAJOR REVISION 26 Apr 2021

Dear editor
In addition to the valuable points raised by the reviewers, it should be emphasized that no data on the vascularity and flow characteristics of nodules are presented in this article. Therefore, according to the criteria presented for Kwark TIRADS, these data must be added. Without these data, no additional information is available in this study.

Editor-in-Chief

MAJOR REVISION 26 Apr 2021

Dear authors,
Your article needs Major Revision.
Regards

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Kavous Firouznia, Prof.
Editor in Chief, Iranian Journal of Radiology

Dear Editor,

Thank you very much for your letter about our manuscript, entitled “Using an Easily Applicable Thyroid Imaging Reporting and Data System (TIRADS) Classification: Our Kwak TIRADS Experience" (Manuscript ID: 111481). We have uploaded our revised manuscript for possible publication in Iranian Journal of Radiology. The study is original and has not been published or under consideration elsewhere. The manuscript was revised thoroughly taking into account your suggestions and comments. Each comment has been carefully considered point by point and responded.
Responses to the reviewers and changes in the revised manuscript are as follows.

REVIEWER1 COMMENTS:

-General Comment: ***About this manuscript it must be said that according to methodology point of view, it written relatively appropriate; but it needs some revisions as follows:***

RESPONSE: Thank you for your thorough review and comments. The manuscript was revised thoroughly taking into account your suggestions and comments. The changes are highlighted in yellow in the manuscript.

1. Each word such as US firstly must be written in full format.

RESPONSE: Necessary changes have been made.

2. The design of study is cross-sectional and it must be written in the first sentence of method section in the abstract and full-text.

RESPONSE: We have modified the abstract and the methods based on your suggestion.

3. İnclusion and exclusion criteria must be mentioned as detailed in the method.

RESPONSE: We have described detailed inclusion and exclusion criteria in the methods section. Also, we have added a diagram to demonstrate the case selection process (Figure 1).

4. Demographic characteristics of patients must be presented in the first paragraph of results.

RESPONSE: Demographic features are now written in the first paragraph of the results.

5. İn table 1, it must be presented demographic characteristics of all patients.

RESPONSE: Table 1 has been modified to include demographic characteristics of all patients based on their diagnosis (benign vs. malignant), and also a separate column summarizes the demographic characteristics of the entire study group.

6. İn table 2, rather than p-value presentation in univariate and multivariate analysis, it is better to be used of odds ratio (OR) along with %95 confidence intervals; moreover, OR also must be presented in the text section of results. Finally, it must be reported the coefficient of determination (R2) for multivariate model in bellow of table 2.

RESPONSE: The results of univariate and multivariate logistic regression analyses are given in Table 4 and the statistical values such as odds ratio or R2 have been added to the table per your recommendation.

REVIEWER 2 COMMENTS:

RESPONSE: Thank you for your thorough review and comments. The manuscript was revised thoroughly taking into account your suggestions and comments.

1-English literature revision of the study is necessary.

RESPONSE: References have been updated in accordance with your suggestion.

2-Please include more images of correlated histology/sonography features of other studied nodules.

RESPONSE: We have updated the figures based on your suggestion.

3-Please write down some demographic features of thyroid nodules in first paragraph of the discussion section.

RESPONSE: We have discussed the demographic features of the study group in the first paragraph of discussion section briefly: "Thyroid nodules are increasingly being recognized due to more easily access to imaging techniques such as US (13, 14). Thyroid nodules are detected in 20% - 76% of the healthy individuals (15, 4), and they are five times more common in women compared to men (16). However, most of these nodules are benign. In the present study, although F:M ratio was 4:1, we did not observe a significant association between gender and malignancy, similar to Kwak et al's findings (9). On the other hand, our malignant cases were significantly older than the benign cases, inconsistent with the literature (9, 10), which may be a reflection of populational differences."

4-Please write down more about importance of Kwak TIRADS in conclusion and discussion sections based on your study results.

RESPONSE: The importance of adopting a standardized reporting system such as Kwak-TIRADS has been emphasized in discussion and conclusion: "In conclusion, US-FNAB is important in distinguishing malignant nodules from benign nodules and preventing unnecessary surgical interventions. However, the decision of US-FNAB by the clinicians may cause unnecessary FNAB. Radiologists should assess the above-mentioned five criteria by ultrasonography and use Kwak-TIRADS

classification by specifying these criteria in the US report. Our results indicate that Kwak-TIRADS classification, which allows ultrasonographic characterization of the thyroid nodules, is correlated with cytopathologic evaluation. We think that adopting Kwak-TIRADS classification will increase communication between radiologists and clinicians. Also, we believe that with the widespread use of the Kwak-TIRADS classification will provide a better selection of patients that will undergo FNAB, and the fact that our results are compatible with the literature suggests that it may be easily adopted to daily practice worldwide. We recommend the use of Kwak-TIRADS for all mentioned reasons."

REVIEWER 3 COMMENTS:

This paper lacks the qualification to be published for the following reasons:

1-Correlation between TIRADS based on radiologic evaluation and histopathologic findings has already been performed in multiple studies with larger sample size then this study already indicating that risk of malignancy increases as TIRADS score increases.

2-What is the logic behind this study that has fewer sample size and specially fewer malignant nodules compared to previous studies??? Since number of malignant nodules (only 42) is extremely low results of this study does not meet the qualification to be published.

3-Other then lack of novelty and lower sample size compared to previous studies there are some other concerns in this paper that i would like authors to take into consideration:

RESPONSE: We thank you for your comments. We have addressed the limitations of our study at the end of the discussion. However, we also think that, despite the limitations, our paper will contribute to the

literature by supporting the use of standardized reporting systems (Kwak-TIRADS classification in this case) while evaluating thyroid ultrasonography, and that our study also suggests that Kwak-TIRADS classification is a practical and reliable classification to be used by radiologists in divergent population settings, given that our study group represents a different population (Turkey) than the previously reported series published on the subject.

Methods

Radiologic Characterization of Nodules;

-Paragraph 1, sentence 3:

The sentence " However, the contribution of size to malignancy and when the nodule was not followed up ,thecontribution of difference in size to malignancy was not investigated " does not have a clear understanding toreaders.

RESPONSE: This sentence has been modified as "However, the association between the changes in the nodule size during follow-up and malignancy was not investigated.".

-Paragraph 1 , sentence 11 :

The phrase " Their shapes were grouped based as taller then wide and taller then wide based on the length of theirvertical and horizontal axes should be rephrased as taller then wide and wider then tall instead.

RESPONSE: This sentence has been modified as "Their shapes were grouped based as taller-than-wide or wider-than-tall based on the length of their vertical and horizontal axes."

Results;

Paragraph 1,sentence 2 :

What do authors mean by "80 patients with Bethesda 3 (AUS-FLUS) and 4 lesions were excluded from statisticalanalysis?

RESPONSE: We did not include patients with Bethesda 3 or 4 cytology to the study. In order to prevent any confusion, we have described the inclusion and exclusion criteria in the methods section in the revised manuscript (highlighted in yellow in the text and also summarized in Figure 1) and we deleted this sentence from the results.

Paragraph 3 , sentence 1-4 : Authors have mentioned "In univariate analysis ,the presence of solid component ,hypoechogenicity, andmicrolobulated or irregular margins ,microcalcifications and taller then wide shape were significantly associated withmalignancy". Right afterwards they mentioned " However , only hypoechogenicity and taller then wide shape werefound to have significant association with malignancy !!!I think authors should add multivariate analysis before the recent sentence.

RESPONSE: Requested change has been made and written in the last paragraph of results section: "Table 4 summarizes the results of uni- and multi-variate logistic regression analyses, the adjusted R^2 value for the model was 0.519. Shape, composition, echogenicity, margin characteristics and presence of calcification were significantly associated with malignancy in the univariate logistic regression analysis (P <0.05), as solid, hypo-echoic, microlobulated-irregular, calcified and taller-than-wide nodules were significantly more likely to be malignant (see the odds ratios in Table 4). On the other hand, only hypoechogenicity (odds ratio: 1.38, 95% CI 1.39 - 10.86; P = 0.01) and taller-than-wide shape (odds ratio: 1.58, 95% CI 1.71 - 20.08; P = 0.005) were found to be associated with malignancy in the multivariate analyses (Table 4)."

Discussion ;
Paragraph 1 , sentence 2 & 3 :
Authors have mentioned that " The difference with Kwak TIRADS was that it included the vascularization of thenodule ". In the

methods authors indicated that they used Kwak TIRADS in this study, however i did not see any resultsbased on vascularization of nodule in this study!!!

RESPONSE: In our opinion, one of the advantages of using Kwak TIRADS classification is that it does NOT involve evaluation of vascular features. Because we think that assessment of vascularization requires both experience and superior technical adjustments, which may not be provided in every hospital setting. However, we understand that the mentioned sentence caused confusion about the inclusion of vascularization assessment in the Kwak TIRADS classification. Thus, we have re-written the mentioned part as "Horvath et al., who first started using the TIRADS classification, based the TIRADS classification on similar US features. However, they examined the vascularization of the nodule as well, unlike Kwak (3). Assessment of nodule vascularization may be somehow problematic as it differs among users and its use has become more complicated in time requiring device-dependent technical adjustments.".

If the reviewer thinks that this modification is not adequate to improve the mentioned discussion, we are willing to further discuss this aspect and to make more changes.

Associate Editor's Comments:

Associate Editor 1:

1- In addition to valuable points of reviewers, it should be emphasized that no data about vascularity and flow characteristics of nodules presented in this article, so, according to criteria presented for Kwark TIRADS, it must be added to data. Without these, no additional information is available in this study.

RESPONSE: Thank you very much for your valuable review. Since Kwak TIRADS classification does not involve assessment of vascularity in the nodule, no data on this aspect is available. In our opinion, one of the

advantages of using Kwak-TIRADS classification is that it does not involve evaluation of vascular features. Because we think that assessment of vascularization requires both experience and superior technical adjustments, which may not be provided in every hospital setting. The assessment of nodule vascularization differs among users and is mostly device-dependent. Therefore, in this manuscript we simply aimed to deliver the message that practical classifications such as Kwak-TIRADS classification should be standardized to be used in every setting around the world. Despite the limitations of the study design, which we mentioned at the end of discussion, we think that our study group represents a different population (Turkey) than the previously reported series published on the subject, supporting that Kwak-TIRADS classification is an easily applicable tool in daily practice in different countries. If the editor thinks that current revision of the text is not clear for the readers, we are willing to further discuss this aspect and to make more changes.

2 Revision 1

4 comments · 19 May 2021 – 5 Sep 2021

Referee 1 Reviewer — ACCEPT — 19 May 2021

Thanks to the dear authors for the revision. Currently, the draft of the manuscript is acceptable in terms of methodology.

Referee 2 Reviewer — MAJOR REVISION — 30 Jun 2021

I have already reviewed this paper.
Besides highlighting changes in the text, the authors are advised to also provide a document responding to reviewer comments in order to proceed further.
Thank you

Associate Editor — ACCEPT — 3 Jul 2021

Dear chief editor
In light of the reviewers' comments, the article can now be published.

Editor-in-Chief — MINOR REVISION — 5 Sep 2021

Dear authors,
Your article needs Minor Revision.
Regards

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Kavous Firouznia, Prof.
Editor in Chief, Iranian Journal of Radiology

Dear Editor,

Thank you very much for your letter about our manuscript, entitled “Using an Easily Applicable Thyroid Imaging Reporting and Data System (TIRADS) Classification: Our Kwak TIRADS Experience" (Manuscript ID: 111481). We have uploaded our revised manuscript for possible publication in Iranian Journal of Radiology. The study is original and has not been published or under consideration elsewhere. The manuscript was revised thoroughly taking into account your suggestions and comments. Each comment has been carefully considered point by point and responded.

Associate Editor's Comments:

Associate Editor 1:
Regarding to comments of reviewers, the article at now can be published.

RESPONSE: Thank you very much for your valuable review.

Associate Editor 2:
1-please change analyzes to analyses.
2-please add full term of abbreviations in the first usage.in addition, please introduce BIRADS in line 150 not line 228.
3-in line 167, effect is not appropriate. It seems better to be efficacy.
4- please change malign to malignant in table 1.
5-in figure 3 legend, the authors mentioned: “US scans demonstrating A-C) Isoechoic TIRADS 4b nodule with solid component,” while the parts B and C are not US scans. Please clarify the aprts in legend and relates parts to texts appropriately.

RESPONSE: Thank you for your thorough review and comments. The manuscript was revised thoroughly taking into account your suggestions and comments. The changes are highlighted in yellow in the manuscript.

3 Revision 2

1 comment · 11 Sep 2021

Editor-in-Chief

ACCEPT 11 Sep 2021

Dear authors,
Your article is acceptable for publication in IJR.
Regards